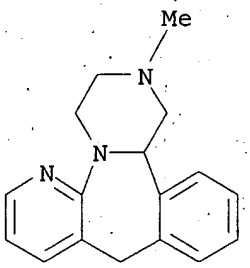
N 85650-52-8 REGISTRY
CN Pyrazino[2,1-a]pyrido[2,3-c][2]benzazepine, 1,2,3,4,10,14b-hexahydro-2-methyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Pyrazino[2,1-a]pyrido[2,3-c][2]benzazepine, 1,2,3,4,10,14b-hexahydro-2-methyl-, (.+-.)-
OTHER NAMES:
CN 6-Azamianserin
CN Mepirzapin
CN Mepirzepine
CN **Mirtazapine**
CN Mirtazepine
CN Mirtazipine
CN Org 3770
CN Promyrtil
CN Remergil
CN Remergon
CN Remeron
CN Rexer
CN Zispin
FS 3D CONCORD
DR 61337-67-5, 82601-27-2
MF C17 H19 N3
CI COM
SR Commission of European Communities
LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, PHAR, PIRA, PROMT, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

289 REFERENCES IN FILE CA (1957 TO DATE)
7 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
289 REFERENCES IN FILE CAPLUS (1957 TO DATE)

=> file medicine

ACCESSION NUMBER: 1996158818 EMBASE
DOCUMENT NUMBER: 1996158818
TITLE: Mirtazapine. A review of its pharmacology and therapeutic potential in the management of major depression.
AUTHOR: Davis R.; Wilde M.I.
CORPORATE SOURCE: Adis International Limited, 41 Centorian Drive,Mairangi Bay, Auckland 10, New Zealand
SOURCE: CNS Drugs, (1996) 5/5 (389-402).
ISSN: 1172-7047 CODEN: CNDREF
COUNTRY: New Zealand
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Mirtazapine is a tetracyclic antidepressant with a novel mechanism of action; it increases noradrenergic and serotonergic neurotransmission via **blockade** of central .**alpha**.2-adrenergic auto- and heteroreceptors. The increased release of serotonin (5-hydroxytryptamine; 5-HT) stimulates serotonin 5-HT1 receptors because mirtazapine directly **blocks** 5-**HT2** and **5-HT3** receptors. The enhancement of both noradrenergic- and 5-HT1 receptor-mediated neurotransmission is thought to be responsible for the antidepressant activity of mirtazapine. In short term (5 to 6 weeks) clinical trials in patients with depression, mirtazapine produces clinical improvements significantly superior to those of placebo, similar to those of tricyclic antidepressants (TCAs) [amitriptyline, clomipramine and doxepin] and possibly superior to those of trazodone. Short term clinical tolerability data suggest that mirtazapine produces fewer anticholinergic-, adrenergic- and serotonergic-related adverse events than TCAs. In rare cases, mirtazapine, in common with many antidepressants, was associated with potentially serious changes in haematological parameters (e.g. agranulocytosis and neutropenia). The drug appears to be safe in overdose and possesses a very low propensity for inducing seizures. Comparisons with other classes of antidepressants are needed to determine the relative position of mirtazapine in clinical practice. However, preliminary data indicate that mirtazapine, with its novel mechanism of action, is a promising addition to currently available options for the treatment of depression.

file

ACCESSION NUMBER: 1998:426105 HCAPLUS
DOCUMENT NUMBER: 129:225564
TITLE: Characterization of enhanced behavioral responses to L-DOPA following repeated administration in the 6-hydroxydopamine-lesioned rat model of **Parkinson**'s disease
AUTHOR(S): Henry, Brian; Crossman, Alan R.; Brotchie, Jonathan M.
CORPORATE SOURCE: Manchester Movement Disorder Laboratory, Division of Neuroscience, School of Biological Sciences, University of Manchester, Manchester, M13 9PT, UK
SOURCE: Experimental Neurology (1998), 151(2), 334-342
CODEN: EXNEAC; ISSN: 0014-4886
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Long-term treatment of **Parkinson**'s disease with dopamine-replacing agents such as L-3,4-dihydroxy-phenylalanine (L-DOPA) is compromised by many side-effects, most notably involuntary movements, L-DOPA-induced dyskinesia. Acute challenge with dopamine-replacing drugs elicits a rotational response in the 6-hydroxydopamine (6-OHDA)-lesioned rat model of **Parkinson**'s disease. This rotation is contraversive to the lesion and is considered to represent an antiparkinsonian effect. More recently, it has become clear that the rotational response shows plasticity and that repeated L-DOPA or apomorphine therapy is accompanied by a marked enhancement in this response. In this study, the authors demonstrate that the enhanced behavioral response to repeated dopamine-replacement therapy seen in the 6-OHDA-lesioned rat has pharmacol. characteristics similar to L-DOPA-induced dyskinesia seen in MPTP-lesioned primates and man. Thus, the magnitude and rate of development of the enhanced response to L-DOPA treatment is related to both the no. of doses and the size of the dose of L-DOPA administered. In contrast, de novo administration of dopaminergic drugs that are assocd. with a lower incidence of dyskinesia, e.g., bromocriptine or lisuride, does not lead to an enhanced behavioral response following repeated treatment. However, following a single "priming" administration of apomorphine, the rotational response elicited by subsequent bromocriptine administrations is enhanced with repeated treatment. Once established, the enhanced behavioral response to repeated L-DOPA-administration (6.5 mg/kg, twice daily) can, like L-DOPA-induced dyskinesia in man and MPTP-treated monkeys, be selectively reduced by coadministration of L-DOPA with the **alpha2**-adrenergic receptor **antagonist** yohimbine (10 mg/kg, -95%), the **5-HT**

uptake **inhibitor** 6-MDOT (2 mg/kg, -90%), or the a-adrenergic receptor antagonist propranolol (10 mg/kg, -35%). While these rats do not exhibit symptoms of dyskinesia per se, this rodent model does exhibit behaviors, the underlying mechanism of which is likely to be similar to that underlying L-DOPA-induced dyskinesia and may prove useful in studying the mol. and cellular mechanisms of L-DOPA-induced dyskinesia in **Parkinson**'s disease.. (c) 1998 Academic Press.

CC 1-11 (Pharmacology)

ST behavior sensitization DOPA **parkinsonism** dyskinesia; dopaminergic drug behavior sensitization **parkinsonism** dyskinesia

IT Antiparkinsonian agents
Dopamine agonists
(characterization of enhanced behavioral responses to L-DOPA and other dopaminergic drugs following repeated administration in hydroxydopamine-lesioned rat model of **Parkinson**'s disease in relation to induction of dyskinesia)

IT Toxicity
(drug; characterization of enhanced behavioral responses to L-DOPA and other dopaminergic drugs following repeated administration in hydroxydopamine-lesioned rat model of **Parkinson**'s disease in relation to induction of dyskinesia)

IT Nervous system
(dyskinesia; characterization of enhanced behavioral responses to L-DOPA and other dopaminergic drugs following repeated administration in hydroxydopamine-lesioned rat model of **Parkinson**'s disease in relation to induction of dyskinesia)

IT Behavior
(rotational; characterization of enhanced behavioral responses to L-DOPA and other dopaminergic drugs following repeated administration in hydroxydopamine-lesioned rat model of **Parkinson**'s disease in relation to induction of dyskinesia)

IT Behavior
(sensitization; characterization of enhanced behavioral responses to L-DOPA and other dopaminergic drugs following repeated administration in hydroxydopamine-lesioned rat model of **Parkinson**'s disease in relation to induction of dyskinesia)

IT 58-00-4, Apomorphine 7101-51-1, L-DOPA methyl ester 19875-60-6 25614-03-3, Bromocriptine
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(characterization of enhanced behavioral responses to L-DOPA and other dopaminergic drugs following repeated administration in hydroxydopamine-lesioned rat model of **Parkinson**'s disease in relation to induction of dyskinesia)

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ACCESSION NUMBER: 1991:74612 HCAPLUS
DOCUMENT NUMBER: 114:74612
TITLE: A novel in vivo test for drugs affecting central serotonergic and adrenergic systems
AUTHOR(S): Rawlow, Andrew; King, Roger G.
CORPORATE SOURCE: Dep. Pharmacol., Monash Univ., Clayton, 3168, Australia
SOURCE: European Journal of Pharmacology (1990), 191(3), 263-72
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In urethane anesthetized rats, **myoclonic** twitches of the anterior digastricus muscle were evoked by L-5-hydroxytryptophan (L-5-HTP, 50-100 mg/kg i.v.), the serotonin (5-HT) receptor agonist, quipazine (1-8 mg/kg i.v.) and the 5-HT releaser, fenfluramine (4-8 mg/kg i.v.). The effect of L-5-HTP or quipazine on the frequency of twitches was **inhibited** by the **5-HT** receptor **antagonist** cyproheptadine. Also L-DOPA (100 mg/kg i.p.) or the .alpha.1-adrenoceptor agonist, cirazoline (0.3-3 mg/kg i.v.) evoked twitches of the muscle which were inhibited by the .alpha.1-adrenoceptor antagonist, prazosin. In decerebrate, artificially respired rats, neither L-5-HTP nor L-DOPA evoked the twitches. The frequency of twitches evoked by fenfluramine but not by L-DOPA was increased by the .alpha.2-adrenoceptor agonist, clonidine (0.2 and 0.4 mg/kg i.v.); clonidine's effect was abolished by the **.alpha.2** -adrenoceptor **antagonist**, yohimbine. The .beta.2-adrenoceptor agonist, salbutamol (0.01-1 mg/kg i.v.) had no effect on fenfluramine-induced twitches. It is concluded that (1) activation of 5-HT receptors or .alpha.1-adrenoceptors in the brain of urethane-anesthetized rats evokes twitches of the anterior digastricus muscle, and (2) this prepn. can be utilized as a test to study the action of compds. on central 5-HT and adrenergic systems.

CC 1-1 (Pharmacology)